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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/065,456	10/19/2002	Toshio Kawai	20.001-AG	4033

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JUDGE PATENT FIRM
RIVIERE SHUKUGAWA 3RD FL.
3-1 WAKAMATSU-CHO
NISHINOMIYA-SHI, HYOGO, 662-0035
JAPAN

EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/065,456	KAWAI, TOSHIO	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-17* is/are pending in the application.

4a) Of the above claim(s) *1-3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/19/2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, Claims 4-17, in the reply filed on November 21, 2005 is acknowledged.

Specification

The disclosure is objected to because of the following informalities:

Page 17 is blank.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 4-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haff et al. (EP 0 636 413 A2).

With regard to Claim 4, Haff et al. disclose an apparatus for continuous amplification of DNA (Figure 1; Columns 9-12, for example), comprising: a

reaction-mixture tank for holding a reaction mixture containing DNA fragments and a reagent solution (Column 10, Lines 40-55, for example); a denaturing isothermal tank for holding a heat-exchange fluid adjusted to a temperature for dissolving apart the DNA'S double strands (Figure 1; Column 10, Lines 1-10, for example); an annealing isothermal tank for holding a heat-exchange fluid adjusted to a temperature at which primers contained in the reagent solution anneal to the DNA fragments (Figure 1; Column 10, Lines 1-10, for example); an elongation isothermal tank for holding a heat-exchange fluid adjusted to a temperature at which complementary chains are extended continuously onto the primers (Figure 1; Column 10, Lines 1-10, for example). It is noted that Figure 1 discloses only two temperature zones, however, Haff et al. expressly discloses that three temperature stable liquid baths may be used for three separate incubation temperatures (Column 9, Lines 30-40, for example). Furthermore, the instant claim language does not recite that the annealing/extension reactions cannot take place in the same tank. Thus, the disclosure of Haff et al. does suggest the apparatus set forth in the instant claim language.

Haff et al. further discloses a circulation-path system through which the reaction mixture in the reaction-mixture tank is fed and guided, the circulation-path system being arranged such that it circuits from the reaction-mixture tank and goes by way of the denaturing isothermal tank, the annealing isothermal tank (Figure 1; Column 10, Lines 25-45, for example); and a pump working to feed the reaction mixture in said circulation-path system unidirectionally through it (Figure 1; Column 15-30, for example); wherein the apparatus is configured such that the

reaction mixture in said circulation-path system is for timed intervals maintained at prescribed temperatures determined by the heat-exchange fluids in the isothermal tanks (Column 12, Lines 1-20, for example).

Haff et al. does not expressly disclose that the *same* reaction mixture is cycled through the temperature zones of the apparatus in Figure 1, however, Haff et al. does disclose one amplification reaction mixture cycled through different temperature zones multiple times in Figure 2.

Based on the combined disclosures of the applied reference, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success modifying the continuous nucleic acid amplification apparatus disclosed in Figure 1 of Haff et al. to incorporate the flowing of the same reaction mixture through the apparatus of Figure 1 multiple times. The motivation to do so, provided by Haff et al., would have been to continuously amplify the same reaction mixture through multiple amplification cycles.

It is noted that the use of the term "tank" does not patentably distinguish the present invention from the disclosure of Haff et al. even though the present invention appears to be a large-scale amplification apparatus. Furthermore, a practitioner of ordinary skill in the art would have recognized that the apparatus disclosed by Haff et al. could have been "scaled-up" to produce larger amounts of amplification product.

At the time of invention, the disclosure of Haff et al. clearly would have provided the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious

to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

With regard to Claim 5, Haff et al. disclose commercially available thermostatted baths that can regulate the bath temperature (Column 11, Lines 50-55, for example) by employing mixer blades (Column 10, Lines 1-10, for example).

With regard to Claim 6, Haff et al. disclose a heating device containing a pump for circuit-feeding the heat-exchange fluid in between the container body and the heating device, and a heat source for heating the heat-exchange fluid to and retaining it at prescribed temperatures, wherein said heating device supplies the heat-exchange fluid to said container body (Figure 3; Column 14-16). A practitioner of ordinary skill in the art would have recognized that the heating elements above could have been incorporated into the apparatus disclosed in Figure 1 of Haff et al.

With regard to Claims 7-9, Haff et al. disclose a *single* continuous reaction tube passing through temperature zones (Figure 1; Column 10, Lines 25-45, for example), however, a practitioner of ordinary skill in the art would have recognized that additional tubes could have been incorporated into the apparatus disclosed in Figure 1 of Haff et al to control reaction time.

With regard to Claims 10-12, Haff et al. disclose that additional baths could be added to increase the number of incubation temperatures (Column 4, Lines 5-10, for example).

With regard to Claims 13-17, Haff et al. disclose a looped capillary tubing whrerein the number of loops is directly related to the number of cycles (i.e. time of total amplification reaction) (Columns 13 and 14). Furthermore, they disclose that the length of tubing is directly related to the residence time of the reaction mixture in each temperature zone. A practitioner of ordinary skill in the art would have recognized that coiled tubing could have been incorporated into the apparatus disclosed in Figure 1 of Haff et al to control residence time of the reaction mixture in each temperature zone.

2. Claims 4, 5, and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Corbett et al. (U.S. 5,270,183) in view of Narang Medical Ltd. (See web included web address).

With regard to Claim 4, Corbett et al. disclose an apparatus for continuous amplification of DNA (Figure 1; Columns 7-8, for example), comprising: a reaction-mixture tank for holding a reaction mixture containing DNA fragments and a reagent solution (Figure 1; Column 7, Lines 60-67, for example); a denaturing isothermal tank for holding a heat-exchange fluid adjusted to a temperature for dissolving apart the DNA'S double strands (Figure 1; Column 8, Lines 1-35, for example); an annealing isothermal tank for holding a heat-exchange fluid adjusted to a temperature at which primers contained in the reagent solution anneal to the DNA fragments (Figure 1; Column 8, Lines 1-35, for example); an elongation isothermal tank for holding a heat-exchange fluid

adjusted to a temperature at which complementary chains are extended continuously onto the primers (Figure 1; Column 8, Lines 1-35, for example). It is noted that Corbett et al. discloses that the individual temperature zones may be fluid-filled baths maintained thermostatically at the required temperature (Column 10, Line 20-25).

Corbett et al. further discloses a circulation-path system through which the reaction mixture in the reaction-mixture tank is fed and guided, the circulation-path system being arranged such that it circuits from the reaction-mixture tank and goes by way of the denaturing isothermal tank, the annealing isothermal tank (Figure 1; Column 10, Lines 25-45, for example); and a pump working to feed the reaction mixture in said circulation-path system unidirectionally through it (Figure 1; Column 15-30, for example); wherein the apparatus is configured such that the reaction mixture in said circulation-path system is for timed intervals maintained at prescribed temperatures determined by the heat-exchange fluids in the isothermal tanks (Column 12, Lines 1-20, for example).

Corbett et al. does not expressly disclose recirculating the same reaction mixture through the entire apparatus in Figure 1 multiple times, however, Corbett et al. does disclose one amplification reaction mixture cycled through different temperature zones multiple times.

Based on the combined disclosures of the applied reference, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success modifying the continuous nucleic acid amplification apparatus disclosed in Figure 1 of Corbett et al. to incorporate recirculating the

same reaction mixture through the entire apparatus in Figure 1 multiple times. The motivation to do so, provided by Corbett et al., would have been to continuously amplify the same reaction mixture through multiple amplification cycles.

It is noted that the use of the term "tank" does not patentably distinguish the present invention from the disclosure of Corbett et al. even though the present invention appears to be a large-scale amplification apparatus. Furthermore, a practitioner of ordinary skill in the art would have recognized that the apparatus disclosed by Corbett et al. could have been "scaled-up" to produce larger amounts of amplification product.

At the time of invention, the disclosure of Corbett et al. clearly would have provided the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

With regard to Claim 5, Corbett et al. disclose thermostatted baths that can regulate the bath temperature (Column 10, Lines 20-25). Thermostatted baths equipped with heating and stirring elements were well-known in the art at the time of invention as demonstrated by Narang Medical Ltd. (http://narang.com/laboratory_equipments/water_bath.php). A practitioner of ordinary skill in the art at the time of invention would have recognized that the thermostatted baths were capable of use with the apparatus disclosed in Figure 1 of Corbett et al. to control temperature.

With regard to Claims 7-9, Corbett et al. disclose a *single* continuous reaction tube passing through temperature zones (Figure 1; Column 10, Lines 25-45, for example), however, a practitioner of ordinary skill in the art would have recognized that additional tubes could have been incorporated into the apparatus disclosed in Figure 1 of Corbett et al to control reaction time.

With regard to Claims 10-12, Corbett et al. disclose a plurality of temperature zone (Column 3, Lines 20-35, for example). A practitioner of ordinary skill in the art would have recognized that additional temperature zones could have been incorporated into the apparatus disclosed in Figure 1 of Corbett et al. to control reaction time.

With regard to Claims 13-17, Corbett et al. disclose a looped capillary tubing wherein the number of loops is directly related to the number of cycles (i.e. time of total amplification reaction) (Figure 1; Column 6, for example). A practitioner of ordinary skill in the art would have recognized that coiled tubing could have been incorporated into the apparatus disclosed in Figure 1 of Corbett et al to control residence time of the reaction mixture in each temperature zone.

3. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Corbett et al. (U.S. 5,270,183) in view of Haff et al. (EP 0 636 413 A2).

The methods of Corbett et al. have been outlined in the above rejections.

With regard to Claim 6, Haff et al. disclose a heating device containing a pump for circuit-feeding the heat-exchange fluid in between the container body

and the heating device, and a heat source for heating the heat-exchange fluid to and retaining it at prescribed temperatures, wherein said heating device supplies the heat-exchange fluid to said container body (Figure 3; Column 14-16). A practitioner of ordinary skill in the art would have recognized that the heating elements above were capable of use with the apparatus disclosed in Figure 1 of Corbett et al.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

Conclusion

Claims 4-17 are rejected. No claims are allowed.

Haff et al. (U.S. 5,720,923), Usui et al. (JP 04-325080), and Larzul (U.S. 5,176,203) are made references of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

2/1/06

Christopher M. Babic
Patent Examiner
AU 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

2/6/06